997-91 Glycogen Loading In Vivo Reverses Decreased Function After Ischemic Preconditioning In Vitro

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We recently observed that glycogen loading of the heart *in vivo* improves ischemia tolerance to the same extent as ischemic preconditioning (IP). We have now tested the hypothesis that glycogen loading is beneficial in a protocol where IP *per se* is not effective. We perfused hearts from fed animals with bicarbonate buffer containing glucose (10 mM). Five min IP with 5 min preconditioning-reperfusion (IP5/5) or 10 min normoxic perfusion (Control, C) were preceded by a 15 min stabilization period and followed by 15 min global, no flow ischemia witl 30 min of reperfusion. Glycogen loaded hearts came from fasted animals, were perfused with buffer containing glucose (10 mM), lactate (10 mM) and insulin (10 mU/ml) and were subjected to the same protocol as IP5/5. Cardiac power and heart rate were assessed continuously. Postischemic recovery was assessed by postischemic power as % of preischemic power. Hearts were freeze-clamped for metabolites. *Results:* Glycogen levels *in vivo* were higher in the glycogen loaded hearts than in C (140 ± 4.5 vs. 70 ± 6.6 μmol/g dry). IP5/5 did not improve postischemic recovery compared to C (68.5 ± 3.7% vs. 71.4 ± 3.5% of preischemic power, n = 9 each). However, glycogen loading of this group resulted in a full return of cardiac power post ischemia (101 ± 6.1%, n = 8). Levels of glucose-6-phosphate (G-6-P), pyruvate, and lactate were not different in IP5/5 and C and returned to preischemic levels with reperfusion. Glycogen loaded hearts maintained elevated G-6-P and lactate levels with reperfusion. *Conclusions:* Glycogen loading improves ischemia tolerance where IP fails to do so. Thus, glycogen or glycogen breakdown may play a crucial role in myocardial protection.

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Wednesday, March 22, 1995, 9:00 a.m.–11:00 a.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: 9:00 a.m.–10:00 a.m.

998-61 Population Prevalence of Wolff-Parkinson-White Syndrome

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Little is known about the epidemiology of Wolff-Parkinson-White (WPW) syndrome in the general population. Virtually all previous studies have been either case series from tertiary care centers or limited to young adult males screened for military training. To date, there are no detailed studies of the prevalence of WPW in the general population. To determine the prevalence of WPW in the general population, we used the Marshfield Epidemiologic Study Area (MESA), a population laboratory of 50,000 people residing in 12 contiguous zip codes in central Wisconsin. Prevalence was determined as of 7/1/91 among MESA residents who had a diagnosis of WPW between 1/1/79 and 6/30/91. Cases were identified by reviewing the medical records and electrocardiograms of: a) all 32 MESA residents with the WPW diagnosis identified by International Classification of Diseases, 9th Revision (ICD-9) Code 426.7 as a hospital discharge or outpatient clinic diagnosis, b) 600 patients with suspected supraventricular arrhythmias identified by three ICD 9 codes, and c) all patients who had an invasive electrophysiology study for overt WPW syndrome in our institution over the last 10 years.

Results: We identified 25 prevalent cases of WPW resulting in an overall population prevalence of 5.1/10,000 (95% C.I., 3.1–7.1).

Age specific-prevalence rates per 10,000 were: 0–19 years — 2.0; 20–39 years — 5.5; 40–59 years — 9.6; >60 years — 4.8. There was no significant difference in males versus females. All 25 verified cases were identified from the 32 potential cases with ICD-9 Code 426.7, indicating that this code is 100% sensitive and has a 78% positive predictive value for WPW syndrome.

Conclusions: 1) The prevalence of WPW in the general population is lower than that reported in selected populations and appears to be highest in those of late middle-age. 2) Based on the findings of our study, we estimate that there are approximately 130,000 individuals in the United States with electrocardiographic documentation of WPW.

998-119 Should We Worry About the Hypercholesterolemic Effects of Anti-Hypertensive Medications?

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Several large studies have demonstrated improved morbidity and mortality with lowering of blood pressure (BP) in hypertension (HTN). The drugs which have been shown to lower BP and cardiovascular (CV) risk are beta blocking agents and thiazide diuretics. In spite of the documented benefit from the use of these agents, there is a tendency among some physicians to avoid these two classes of drugs when treating HTN. One of the reasons quoted is that both of these classes of drugs increase cholesterol levels, which is postulated to negate the CV risk reduction afforded by BP lowering. This study was undertaken to determine the magnitude of benefit from the lowering of BP with these drugs and compare it with the expected loss of benefit due to increased cholesterol levels with these drugs. A decision analysis was constructed utilizing a new life expectancy (LE) function. LIFESPANS (Lagrange Interpolated Functions of Empirical Survival Percentages Approximated by NEVADA Simulations) is designed to individualize mortality prediction utilizing mortality data from the National Center for Health Statistics and numerous large epidemiological studies. Modifiable factors which are included in this model to assist in the survival prediction include: age, sex, race, BP, cholesterol level, current smoking history, and body mass index. For the initial analysis, a 10% reduction in BP with a 5% increase in absolute cholesterol level with these agents was assumed. Sensitivity analyses were performed for a wide range of initial BPs, cholesterol levels and smoking history. Reduction of BP with either of these agents resulted in 1–5 years of additional LE depending on baseline conditions. Significant increases in LE were predicted even in the elderly. A 5% rise in cholesterol, in contrast, was associated with a 0.0–0.6 year decrease in LE. The reduction in LE for increased cholesterol was at most 28% of the increase in LE due to BP lowering. Women had a slightly greater reduction of LE from increased cholesterol. In conclusion, without taking the other metabolic effects of these agents into consideration, the increase in CV risk due to the small predicted increase in cholesterol only partially negates the benefits of BP lowering. These predictions are based on studies utilizing high dose (50–100 mg) diuretics. Lower doses will have even less effect on lipid profiles and the negative LE changes in hypertensive patients.

998-120 Left Ventricular Systolic Performance Changes in Mild Hypertensive Subjects Treated with Antihypertensive Monotherapy or Placebo: The Treatment of Mild Hypertension Study (TOMHS)

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Few large scale studies have evaluated long term effects of antihypertensive monotherapy (MT) versus placebo (P) on left ventricular (LV) systolic performance. Over a period of 4 years, 844 subjects with mild hypertension (mean BP:140/91) without cardiac disease were treated with one of 5 MTs or P, all receiving nutritional-hygienic intervention. 2-D directed M-mode echocardiograms evaluated LV function at baseline, 3 months and annually through 4 years. Average changes over 4 years were compared between combined MT groups and P. Average decrease in BP was 15.9/12.3 mmHg in the MT group and 9.1/8.6 mmHg in the P group. For global systolic performance, stroke volume, ejection fraction, and fractional shortening (FS) increased with MT but decreased in P ($p < 0.01$ (MT vs P). Average change from baseline in stroke volume was −3.0% with P and +1.7% with MT. Cardiac output, stroke work index and minute work index decreased similarly in both MT and P. Peak- and end-systolic stress (ESS) increased significantly more in P than MT ($p < 0.01$). Total peripheral resistance decreased more in the MT group ($p < 0.001$). For indexes of contractility, ESS/ES volume index increased more in the P group, FS/ESS increased in MT and decreased in P, and SBP/ES dimension decreased more in the MT group ($p < 0.02$ for each).

These findings suggest that even in mild hypertensives without underlying LV dysfunction, the addition of MT to nutritional-hygienic therapy can produce small, though significant changes in LV performance characteristics.

998-121 Effect of Hormone Replacement Therapy on Fibrinogen Level in Postmenopausal Women in the Framingham Offspring Study

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Hormone replacement therapy (HRT) is associated with a decreased risk of coronary heart disease (CHD) in postmenopausal women, but the mechanism of its protective effect is not fully characterized. To evaluate the relation-